REMARKS

Claims 1-20 were originally filed and were subject to a Restriction Requirement. Applicants affirm election, with traverse, of original claims 1-5 and 6, corresponding to the invention of Groups I and II. Justification for the amendments is as follows. The claims have been amended to clarify the invention. In particular, claim 1 has been amended to recite "the complement" of the cDNAs, and to recite antigenic epitopes of SEQ ID NO:1, and a naturally occurring variant of SEQ ID NO:1 having at least 90% sequence identity with SEQ ID NO:1. Claims 1 and 2 have also been amended to recite the term "comprising". Support for the amendments to claim 1 are found in the specification, for example, at p. 6, lines 19-21 (complement), at p. 3, line 17, and at p. 8, line 33 through p. 9, line 6 (variants of SEQ ID NO:1), and at p. 10, line 33 through p. 11, line 3 (antigenic epitopes of SEQ ID NO:1). No new matter is added by any of these amendments, and entry of the amendments is respectfully requested.

35 U.S.C. § 112, Second Paragraph, Rejection of Claims 1-6

The Examiner has rejected claims 1-6 under 35 U.S.C. § 112, second paragraph, as being indefinite for filing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that in claim 1, the metes and bounds of cDNA are not clear as to whether the cDNA encodes a protein having residues in addition to SEQ ID NO:1; e.g., do claims 1 and 2 consist of or comprise the recited sequences?

Applicants have amended claims 1 and 2 to recite a cDNA "comprising ---". Withdrawal of the rejection of these claims under 35 U.S.C. § 112, second paragraph is therefore requested.

35 U.S.C. § 112, First paragraph, Rejection of Claims 1-6

The Examiner has rejected claims 1-6 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a was as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make use of the invention. The Examiner stated that applicant asserts that the cDNA and protein are useful in the diagnosis and treatment of disorders associated with inflammation (page 3, lines 7-9). Figure 3A shows that this DNA is expressed in many tissue types and Figure 3B shows that it is expressed in samples from several lymphoid tissues, most with cancer related conditions. However, the Examiner stated, one skilled in the art would have reason to doubt the usefulness of the DNA (or protein) for diagnosis or treatment of diseases or disorders

associated with inflammation and the immune response (list in specification page 19, lines 4-22). There is no guidance as to which diseases or disorders from this long list that there is a particular association because there is no showing in the specification that links a particular disease state to a particular presence of the cDNA. There is no teaching in the specification on the sensitivity or specificity of the diagnostic indication (presence of cDNA). It is not clear, the Examiner stated, if there would be false positives or negatives associated with this test. The Examiner pointed to page 19, line 23 of the specification as indicating that conditions are caused by increased expression of the protein, but it is not clear that this can be differentiated from normal cell or particular diseases or states of disease/disorder progression. The Examiner stated that Figure 3B does not indicate that the detection of the cDNA is from normal or increased expression situations or that it can determine a specific disease or condition, and there are no working examples of diagnosis or treatment.

In response to this rejection, the Examiner is reminded that the utility standard under 35 U.S.C. § 101, and likewise of enablement under 35 U.S.C. § 112, first paragraph, is not an onerous one.

1. The Applicable Legal Standard

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

Applicants first of all submit that there is a well established utility for polynucleotides encoding GRIIP not addressed by the Examiner, based on a high degree of homology between GRIIP and a rat kidney injury associated protein, KIM (HW051). See specification, at page 10 and reference # 5 of the information disclosure statement. KIM is described as associated with kidney injury and therefore useful in the diagnosis of kidney disorders such as acute renal failure or acute nephritis. The specification discloses that such injury is associated with inflammation and that KIM may be an inflammation protein specifically associated with kidney. GRIIP therefore appears to be a similar inflammation-associated

protein with different tissue specificity. This is further supported in the specification by the expression of GRIIP in various inflammatory conditions, including cancer. See page 9, last paragraph, and Figure 3B. The diagnosis of an inflammatory condition, regardless of the specific underlying cause it is associated with is, itself, a specific and substantial utility. One skilled in the art would readily recognize the value of diagnosing and treating such inflammation to reduce further tissue damage while further tests are being conducted to establish the underlying condition. Thus a diagnostic marker for inflammation in a tissue is a specific and substantial utility.

Applicants further submit that the Examiner's allegation that there is no guidance as to which diseases or disorders that there is a particular association (of the cDNA) because there is no showing in the specification that links a particular disease state to a particular presence of the cDNA (of SEQ ID NO:2) is incorrect. The specification asserts the use of the polynucleotides in the diagnosis of diseases of the immune system, and particularly recites cancers of the immune system. See p. 1, lines 6-7 and p. 9, l;ines 10-11. Figure 3B lists all of the 159 cDNA libraries of the hemic and immune system category examined in which the presence of polynucleotides encoding GRIIP were found, except for two normalized and one subtracted library which were excluded from the analysis as possibly under representing the expression of some genes. As described in the specification at page 9, lines 28-32, the majority of these tissues and cell lines are derived from inflamed or cancerous conditions. With regard to specific disease conditions, GRIIP expression is only found in a bone marrow cell line derived from a bone marrow neuroblastoma. It was not found in at least four other bone marrow cDNA libraries unassociated with disease. In adult spleen tissue, GRIIP expression was found only in a spleen tumor cDNA library. Its expression was again not found in at least seven other adult spleen libraries unassociated with disease. The expression of GRIIP in bone marrow or spleen is therefore diagnostic for cancer in these tissues. Applicants have included a declaration under 37 CFR 1.132 by Dr. Michael Walker, an inventor on this application, in support of these uses. In his declaration, Dr. Walker asserts that when used in a tissue specific and clinically relevant manner, GRIIP expression is diagnostic of cancers of the bone marrow or spleen.

Applicants therefore submit that there is both a well established and a specific and substantial asserted utility for the claimed invention that would enable on skilled in the art to use the invention without further undue experimentation, and the Examiner offers no evidence or sound scientific reasoning to the contrary. In fact, the Examiner offers only speculation that with respect to any asserted diagnostic use of GRIIP, there may be "false positives or negatives associated with this test". See Office Action at page 4.

Applicants therefore submit that the Examiner has not met the necessary burden of proof for demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention and request withdrawal of the rejection of claims 1-6 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited. Applicants further request that upon allowance of claims 1 and 3, that claims 7-12 be rejoined and examined as methods of use the the compositions of matter of claim 1 and 3 that depend from and are of the same scope as claims 1 and 3 in accordance with *Ochiai and Brouwer*. See MPEP § 821.04 and the Commissioner's Notice in the Official Gazette of March 26, 1996.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of Record, below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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Version with markings to show changes made

IN THE CLAIMS:

Claims 1 and 2 have been amended as follows:

1. (Once Amended) An isolated cDNA, or the complement thereof, comprising a sequence encoding a protein selected from [having the]:

a) an amino acid sequence of SEQ ID NO:1;

b) an antigenic fragment of SEQID NO:1 from about amino acid residue I18 to about amino acid residue V44, from about amino acid residue T145 to Q154, from about amino acid residue L163 to Q200, or from about amino acid residue Q206 to K277 of SEQ ID NO:1, and

c) a naturally occurring variant of SEQ ID NO:1 having at least 90% sequence identity with the amino acid sequence of SEQ ID NO:1.

2. (Once Amended) An isolated cDNA comprising a sequence selected from:

a) a nucleic acid sequence of SEQ ID NO:2 or the complement thereof;

b) a fragment of SEQ ID NO:2 selected from SEQ ID NOs:3-10 or the complement thereof; and

c) a variant of SEQ ID NO:2 selected from SEQ ID NOs:11-13.